REMARKS

Claims 3-8 are all the claims pending in the application.

Claim 3 has been amended to include a recitation of the particular stage at which the compound of the present invention may be used to treat ischemic stroke, and to include reference to pharmaceutically-acceptable carriers. Support for the former addition can be found at page 6, lines 20-22. Support for the latter addition can be found at page 16, line 25 through page 17, line 6. The term "selective" has also been removed, supported by claim 1 as originally filed.

Claim 4 have been amended to remove the term "selective." Support for this amendment may be found in claim 1, as originally filed.

Claims 6-8 have been amended to incorporate subject matter recited in claims 3-5.

No new matter has been added. Entry of this amendment is earnestly solicited.

I. Formal Matters

As a point of clarification, Applicants note that at page 2 of the Office Action, the Examiner states that claims 3-9 are presented for examination. Applicants respectfully assert that claims 3-8 are all of the claims pending. Indeed, Applicants have never presented a claim 9.

II. Substitute Specification

Applicants submit herewith a Substitute Specification correcting an error made in the translation of the PCT application, written in the Japanese language, into English for entry into the national stage in the United States.

The following explanation of the translation error is reiterated in the enclosed Declaration Under 37 C.F.R. §1.132, executed by one of the inventors of the present invention.

As found throughout the present application, as filed, the term "cerebral infarction" is used to refer to the condition for which the novel medicaments of the present invention are recited (*see* Disclosure of Invention, page 6, lines 5-6). The application also uses the term "cerebral infarction as the acute stage" (*see* page 6, lines 21-22). However, in the course of considering the Examiner's rejections, the inventor Masamichi OKADA noticed that these English terms are not appropriate because the terms do not distinguish the two meanings encompassed within the corresponding Japanese word.

In general, the corresponding Japanese term is used as the name of the disease, i.e., ischemic stroke. Ischemic stroke is a disease caused by an ischemic event which is a condition of oxygen deficiency in part of the brain due to an interruption of blood flow by a thrombotic and/or embolic occlusion of a cerebral artery and causes consequent neurological symptoms. If the occlusion is maintained long enough to induce neuronal damage (longer than 1 hour), an infarct (localized area of irreversible damage due to the occlusion of the artery supplying the area) may form. A continued blood flow interruption can lead to the progression of the infarct to surrounding neuronal cells. Injury of the neuronal cells that control certain function causes the corresponding functional disorders as a sequela in the chronic stage of ischemic stroke.

The period of time shortly after the ischemic event induced by the occlusion of the cerebral artery is termed "acute stage ischemic stroke." If the interruption persists, neuronal tissue begins to be irreversibly damaged, i.e., a cerebral infarct forms. Regions of neuronal damage are referred to as "cerebral infarct" and the pathological condition which exists due to the cerebral infarct is called "cerebral infarction." Thus, after the occlusion of cerebral artery, a

subject is considered to have a disease ("ischemic stroke") that may, if not immediately corrected, lead to a pathological condition ("cerebral infarction").

The Japanese term used in the PCT application has both meanings of the disease ("ischemic stroke") and the pathological condition ("cerebral infarction"). However, as explained above, in the English language, two different terms are used. The literal translation of the Japanese term means "cerebral infarction at the acute stage." Because the term is used for categorizing the disease based on the passage of time, it should have been translated into "acute (stage) ischemic stroke."

The U.S. specification, as filed, provides support for the use of the term "ischemic stroke" at page 6, line 2, where "human ischemic stroke" is disclosed.

Thus, where "cerebral infarction" and "acute stage cerebral infarction" are used in the specification and claims of the present application, the terms "ischemic stroke" and "acute stage ischemic stroke" should more accurately be used, respectively.

The specification and claims have been amended accordingly.

III. Rejection of claim 3 under 35 U.S.C. § 102(b)

At page 2 of the Office Action, claim 3 is rejected under 35 U.S.C. §102(b) as being anticipated by Japanese Patent Application 8-169884 (JPA '884).

The Examiner states that the rejection is based upon the reasons set forth in the Office Action dated January 29, 2001, namely, that JPA '884 allegedly teaches the use of the claimed compounds in a pharmaceutical formulation.

Applicants' Response

Applicants assert that the disclosure of JPA' 884 is limited to suggesting that a mGluR1 antagonist may be useful for improving/treating the after-effects of a cerebral infarction (sequelae caused by cerebral infarction). There is no disclosure in JPA '884 that the mGluR1 antagonist of the present invention has the ability to effectively treat acute stage ischemic stroke, as recited in amended claim 3. Thus, Applicants have identified an important use for the compound of the present invention.

As set forth in detail in the enclosed Declaration Under 37 C.F.R. §1.132, executed by one of the inventors of the present invention, JPA '884 does not anticipate the present invention.[1]

Applicants note that copies of each of the documents referenced in the Declaration are enclosed with the present submission.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Rejection of claims 4-8 under 35 U.S.C. §103

At page 2 of the Office Action, claims 4-8 are rejected under 35 U.S.C. §103(a) as being unpatentable over JPA '884.

The Examiner alleges that JPA '884 teaches mGluR1 antagonists for the treatment of ischemic stroke. The Examiner recognizes that JPA '884 does not disclose Applicants' selective

[1] Please note that the citation for one of the references recited in the Declaration is incorrect. As cited throughout the specification (*see, e.g.*, page 5, lines 6-7), Stroke 352(suppl. III):1-30 (1998) is incorrectly cited as Lancet 352(suppl. III):1-30 (1998).

mGluR1 antagonist. However, the Examiner contends that it would have been obvious to one skilled in the art to substitute one mGluR1 antagonist for another and use it for the same purpose.

Applicants' Response

Applicants respectfully assert that the present invention would not have been obvious to one of ordinary skill in the art in view of JPA '884.

As explained in detail in the enclosed Declaration Under 37 C.F.R. §1.132, executed by one of the inventors of the present invention, neither JPA '884, or any reference cited therein, teaches, suggests or makes obvious the use of a compound exhibiting mGluR1 antagonism in the treatment of acute stage ischemic stroke according to the present invention. Indeed, JPA '884 merely discloses a compound having mGluR1 antagonism that is useful for treating the conditions of sequelae caused by cerebral infarction. There is no disclosure in JPA '884 that a mGluR1 antagonist would be useful in the treatment of acute stage ischemic stroke.

As also explained in detail in the Declaration, the skilled artisan would not have reasonably expected that an agent useful in the treatment of sequelae caused by cerebral infarction sequela would also be useful in the treatment of acute stage ischemic stroke, due primarily to the different goals of each treatment and the completely different physiological effect of the different treatment agents.

And as the Declaration further discusses, the technical level at the time the present invention was made, and the long-felt need in this area of technology, also argue for the non-obviousness of the present invention.

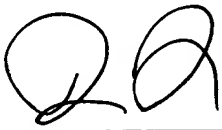
Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

V. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,



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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims are amended as follows:

3. (Twice amended) A pharmaceutical composition for treating acute stage ischemic stroke~~cerebral infarction~~, which comprises a compound having ~~selective~~ mGluR1 antagonism in an amount effective for treating acute stage ischemic stroke as an active ingredient and a ~~in a~~ pharmaceutically-acceptable carrier ~~affective amount~~.

4. (Amended) The pharmaceutical composition according to claim 3, wherein the compound having ~~selective~~ mGluR1 antagonism is 6-amino-N-cyclohexyl-N,3-dimethylthiazolo[3,2-a]benzoimidazole-2-carboxamide dihydrochloride

6. (Amended) A method ~~of treating~~ for treatment of a mammal afflicted with acute stage ischemic stroke, said method ~~a mammal in need of treatment~~ comprising the step of administering a compound having mGluR1 antagonism ~~the pharmaceutical composition according to claim 3~~ to said mammal.

7. (Amended) The ~~A~~ method ~~of treating a mammal in need of treatment comprising the step of administering the pharmaceutical composition~~ according to claim 6~~4~~, wherein said compound is 6-amino-N-cyclohexyl-N,3-dimethylthiazolo[3,2-a]benzoimidazole-2-carboxamide dihydrochloride ~~to said mammal~~.

8. (Amended) The ~~A~~ method ~~of treating a mammal in need of treatment comprising the step of administering the pharmaceutical composition~~ according to claim 6~~5~~, wherein said

compound does not have an agonist or antagonist effect on mGluR2, mGluR3, mGluR4, mGluR6 or mGluR7 ~~to said mammal~~.